## AMENDMENTS TO THE CLAIMS

1. (Original) A method for selecting or designing a compound for modulating the activity of phosphoinositide dependent protein kinase 1 (PDK1), the method comprising the step of using molecular modelling means to select or design a compound that is predicted to interact with the protein kinase catalytic domain of PDK1, wherein a three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 is compared with a three-dimensional structure of a compound, and a compound that is predicted to interact with the said protein kinase catalytic domain is selected, wherein the three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 is a three-dimensional structure (or part thereof) determined for a polypeptide consisting of residues equivalent to residues 51 to 359 of full length human PDK1, or a fragment or fusion thereof.

2. (Original) The method of claim 1 wherein the three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 structure is a three-dimensional structure (or part thereof) determined for a polypeptide consisting of residues 51 to 359 of full length human PDK1 or a fusion thereof.

3. (Original) The method of claim 2 wherein the three-dimensional structure (or part thereof) is determined for a polypeptide consisting of residues 51 to 359 of full length human PDK1 and the amino acid sequence Gly-Pro preceding the methionine corresponding to Met51 of human PDK1.

4. (Original) The method of claim 1 wherein the three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 structure is a three-dimensional structure (or part thereof) determined for a polypeptide consisting of residues 71 to 359 of full length human PDK1 or a fusion thereof.

5. (Currently amended) The method <u>of</u> claim 1 wherein the three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 structure is obtainable by X-ray analysis of a crystal obtainable using a mother liquor solution comprising ammonium sulphate.

6. (Original) The method of claim 5 wherein the mother liquor solution is of pH 7 to 9.

7. (Original) The method of claim 6 wherein the mother liquor solution is of pH 8.5.

8. (Previously presented) The method of claim 7 wherein the mother liquor solution comprises ATP.

9. (Previously presented) The method of claim 1 wherein the three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 structure is that represented by the structure co-ordinates shown in Examples 2, 3 or 4, or 7 or 8, or a structure modelled on such structure co-ordinates.

10. (Previously presented) The method of claim 1 wherein the molecule is predicted to bind to a region of the structure termed the "PIF binding pocket" (formed by residues including residues Lys115, Ile118, Ile119 on the αB helix, Val124, Val127 on the αC helix and Leu 155 on β-sheet 5 of full length human PDK1, or equivalent residues), the "phosphate binding pocket" (formed by residues including residues Lys76, Arg 131, Thr 148 and Gln150 of full length human PDK1, or equivalent residues) and/or the αC helix (residues equivalent to 123-136 of full length human PDK1), or interacting regions.

11. (Previously presented) The method of claim 1 wherein the compound is for modulating the protein kinase activity of PDK1 towards PKB or other PH-domain-comprising/phosphoinositide-binding substrate of PDK1.

12. (Previously presented) The method of claim 1 wherein the compound is for modulating the protein kinase activity of PDK1 towards SGK, S6K or other substrate of PDK1 whose phosphorylation by PDK1 is promoted by phosphorylation of the substrate on the Ser/Thr of the "hydrophobic motif" FXXFS/TY.

13. (Original) A method for selecting or designing a compound for modulating the activity of a hydrophobic pocket (PIF binding pocket)-containing protein kinase having a hydrophobic pocket in the position equivalent to the hydrophobic pocket of human PDK1 that is defined by residues including Lys115, Ile118, Ile119, Val124, Val127 and/or Leu155 of full-length human PDK1 and further having a phosphate binding pocket in the position equivalent to the phosphate binding pocket of human PDK1 that is defined by residues including Lys76, Arg131, Thr148 and/or Gln150, the method comprising the step of using molecular modelling means to select or design a compound that is predicted to interact with the said hydrophobic pocket-containing protein kinase, wherein a three-dimensional structure of a compound is compared with a three-dimensional structure of the said phosphate binding pocket and optionally also the hydrophobic pocket and/or αC helix or region interacting therewith, and a compound

that is predicted to interact with the said phosphate binding pocket and optionally also the hydrophobic pocket and/or αC helix or region interacting therewith, is selected.

14. (Withdrawn) The method of claim 13 wherein the protein kinase is an isoform of Serum and Glucocorticoid stimulated protein kinase (SGK), Protein Kinase B (PKB), p70 S6 kinase, p90 RSK, PKC isoforms (for example PKCα, PKCδ, PKCζ), PRK1, PRK2, MSK1 or MSK2.

15. (Previously presented) The method of claim 13 wherein the three-dimensional structure of said phosphate binding pocket and optionally also the hydrophobic pocket and/or αC helix or region interacting therewith is a structure modelled on the basis of a three-dimensional structure as defined in claim 9.

16. (Previously presented) The method of claim 1 further comprising the step of synthesising, purifying and/or formulating the compound.

17. (Original) A method for assessing the activation state of a structure for a protein kinase, wherein the structure is analysed using principle component analysis of the structure co-ordinates.

18. (Original) The method of claim 17 wherein the activation state of the structure is classified as "open", "closed" or "intermediate".

19-42. (Canceled)